

REMARKS

A. The Status of the Claims and the Amendments

Claims 12, 14, and 24 have been amended. Claim 17 has been canceled without prejudice. New claim 26 has been added. Accordingly, after the amendment has been entered, Claims 12, 14, 16, 18, 21-24, and 26 will be under consideration. The claims amendments clarify the language of the claims and harmonize the language of the claims with the specification.

In particular, the structures of sulfonates 1-11 presented in claim 24, as amended, are disclosed in FIG. 10 of the original specification. Accordingly, it is submitted that the claims amendments do not introduce any new matter. The Applicants also acknowledge the fact that the previous rejections under 35 U.S.C. § 112, first paragraph (enablement and written description) have been withdrawn by the Examiner in view of the arguments previously provided by the Applicants.

B. Rejection Under 35 U.S.C. § 102(b)

Claims 12, 14, 16, 17, and 21 have been rejected under 35 U.S.C. § 102(b), as allegedly being anticipated by Purohit et al. (*Biochemistry*, 1995, 34, 11508-11514) (item 3, page 3 of the Office Action). The rejection is respectfully traversed.

Claims 12 and 14 recite using "the combinatorial chemical library comprising a mixture, the mixture including a plurality of members of the formula $R^*(F - L) - X$ ".

As previously discussed, Purohit et al. fail to teach using a combinatorial chemical library which includes a mixture of plurality of compounds. Purohit et al. only teach using estrone derivatives, but are silent with respect to using their compounds (4)-(6) as a library, i.e., as a mixture. The Examiner has indicated that claims 12 and 14 would have recited novel matter had it been clearly stated that the library members are

“being mixed together” thus precluding the possibility of parallel screening (see, Office Action, page 6, lines 14-21). For instance, the Examiner has indicated that novelty would have been present if the limitation requiring mixing “in the same container” would have been recited (see, Office Action, page 7, lines 1-2).

It is respectfully submitted that reciting “in the same container” is unnecessary to establish that the library members are “being mixed together.” Indeed, each of claims 12 and 14 recites combining the protein mixtures with the members of the combinatorial library “under conditions for reaction of said sulfonyl functional group with active proteins.” Such reaction conditions inevitably include the components being mixed together “in the same container.” Clearly, for the conditions for the reaction to exist, the direct intimate contact between the components is needed, and mixing in the same container is inherently required to establish such a contact.

Accordingly, reconsideration and withdrawal of the rejection of claims under 35 U.S.C. § 102(b) are respectfully requested.

C. Rejection Under 35 U.S.C. § 103(a)

Claims 12, 14, 16-18, and 21-24 have been rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Gygi et al. (*Nature Biotechnology*, 1999, 17(10):994-999), Liu et al. (*PNAS*, 1999, 96(26):14694-14699), and Bogyo et al. (*PNAS*, 1996, 94, 6629-6634)(item 5, page 8 of the Office Action). This rejection is respectfully traversed. None of the cited references, either alone or in combination, disclose or suggest the methods of the present invention.

The Applicants have noticed that the Examiner rejected the 37 CFR § 1.132 declaration as defective. In response, the errors in the original declaration have been corrected. The newly executed declaration refers to the correct patent application, which is the current application No. 09/836,145 and reiterates that the subject matter set forth in Liu et al. was derived from the Applicants’ own work. The Examiner agreed with the

previous argument that under MPEP § 716.10 a 1.132 declaration, stating that the relevant parts of the reference originated with the applicants, is a proper tool for removing the reference.

Accordingly, it is clear that the Liu et al. reference should be removed from the rejection. The Examiner correctly pointed out that attacking references individually is not allowed to show non-obviousness over the combination of the individual references. However, this is not what the Applicants submitted previously. The Examiner would undoubtedly agree that if a combination of references is used, every element of the rejected claim has to be either disclosed or suggested in the combination. What the Applicants respectfully suggest is that such a requirement is not met by using the combination of Gygi et al. and Bogyo et al.

With respect to claims 12 and 14, the combination of Gygi et al. and Bogyo et al. only teaches treating two separate protein samples (disclosed by Gygi et al.) and using the probes with sulfonyl groups (e.g., those derived from vinyl sulfones)(disclosed by Bogyo et al.). The combination of Gygi et al. and Bogyo et al. fail to either teach or to suggest “a combinatorial chemical library, the combinatorial chemical library comprising a mixture, the mixture including a plurality of members of the formula $R^*(F-L)-X$,” where the members of the combinatorial chemical library “react with an active site of said protein member,” as recited in claims 12 and 14.

In addition, vinyl sulfones disclosed by Bogyo et al. do not encompass sulfonates recited in claims 12 and 14 of the present application. It is respectfully submitted that there is no relationship, other than the presence of a sulfur atom, between the structures disclosed by Bogyo et al. and the structures recited in claims 12 and 14. Indeed, sulfones and sulfonates are different reactive moieties in that the sulfur atom of vinyl sulphone is attached to two oxygens and two carbons, whereas in the sulfonates, the sulfur atom is attached to three oxygens and one carbon. Also, in the vinyl sulfones the vinyl portion is the reactive group and the sulfone portion serves only to activate the vinyl group, i.e. the

sulfone group does not directly participate in the reaction. In the sulfonate probes of the present invention, the sulfonate serves as the leaving group, so it is directly a part of the reaction that occurs.

In addition with respect to claim 12 only, the combination of Gygi et al. and Bogyo et al. only teaches using the protein mixture including solely denatured proteins the activity of which have been destroyed (disclosed by Gygi et al.). The combination of Gygi et al. and Bogyo et al. fail to teach or suggest that “conjugates in said active complex mixture absent in said inactivated complex mixture are comprised only of active proteins,” as recited in claim 12.

Accordingly, it is respectfully submitted that the combination of the references provided by the Examiner fails to disclose or suggest every element of claims 12 and 14. Consequently, claims 12 and 14 are shown to be patentably distinguishable over the cited art. Claims 16-18, and 21-24 depend on claim 14 and are patentable for at least the same reasons. Accordingly, reconsideration and withdrawal of the rejection of claims 12, 14, 16-18, 21 and 22-24 under 35 U.S.C. § 103(a) are respectfully requested.

D. Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 12, 14, 16-18, and 21-24 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicants regard as the invention (item 8, page 14 of the Office Action). These rejections are respectfully traversed.

With respect to claims 12 and 14, the term “a peptide of polypeptide” has been amended to “a peptide or polypeptide,” to correct a grammatical error that has been inadvertently made in the original specification.

With respect to claim 24, specific chemical structures of sulfonates 1-11 and 15-17 have been incorporated into the claim, as required by the Examiner.

Accordingly, reconsideration and withdrawal of the rejection of claims 12, 14, 16-18, 21 and 22-24 under 35 U.S.C. § 112, second paragraph, are respectfully requested.

E. Objections Under 37 C.F.R. 1.75(c)

The Examiner objected to claims 17 and 24 due to some alleged informalities (item 7, page 13 of the Office Action). The objections are respectfully traversed. The Applicants have canceled claim 17, without prejudice, thus making the objection to claim 17 moot.

With regard to objection to claim 24, the applicants amended claim 14 and added the limitation "quinoline." This limitation is fully supported by the original specification (see FIG. 10). Accordingly, the Markush listing in claim 24 now does not include any members that are not recited in the broader independent claim 14.

In view of the foregoing, reconsideration and withdrawal of the objections to claims under 37 C.F.R. 1.75(c) are respectfully requested.

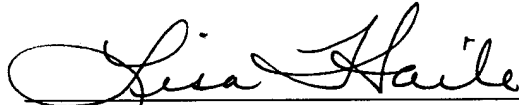
CONCLUSION

In view of the above amendments and remarks, reconsideration and favorable action on all claims are respectfully requested. In the event any matters remain to be resolved, the Examiner is requested to contact the undersigned at the telephone number given below so that a prompt disposition of this application can be achieved.

No fee is deemed due in connection with this response. In case any fee is due, the Commissioner is hereby authorized to charge any other fees associated with the filing submitted herewith, or credit any overpayment, to Deposit Account No. 07-1896.

Respectfully submitted,

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